STIC-ILL

From: STIC-Biotech/ChemLib
Sent: Thursday, October 09, 2003 1:58 PM
To: STIC-ILL
Subject: FW: In re: 10/005, 200 Journal articles

-----Original Message-----
Fr m: Ford, Vanessa
Sent: Thursday, October 09, 2003 1:41 PM
T : STIC-Biotech/ChemLib
Subject: In re: 10/005, 200 Journal articles

Please supply:

SO J EXP MED, (1986) 164 (3), 762-776.

SO VETERINARY MICROBIOLOGY, (NOV 1993) Vol. 37, No. 3-4, pp. 389-395.

SO Microbial pathogenesis, Sept 1999. Vol. 27, No. 3. p. 133-143

SO INFECTION AND IMMUNITY, (NOV 1998) Vol. 66, No. 11, pp. 5399-5405.

Vanessa L. Ford
Biotechnology Patent Examiner
Office: CM1 8A16
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Phone: 703.308.4735
Art Unit:1645

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Sent: Thursday, October 09, 2003 1:58 PM
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Adams Only
20

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From: Ford, Vanessa
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SO Microbial pathogenesis, Sept 1999. Vol. 27, No. 3. p. 133-143

SO INFECTION AND IMMUNITY, (NOV 1998) Vol. 66, No. 11, pp. 5399-5405.

Vanessa L. Ford
Biotechnology Patent Examiner
Office: CM1 8A16
Mailbox: CM1 8E12
Phone: 703.308.4735
Art Unit:1645

Article title	The protective M proteins of the equine group C streptococci
Article identifier	0378113593001389
Authors	Timoney_J_F Mukhtar_M_M
Journal title	Veterinary Microbiology
ISSN	0378-1135
Publisher	Elsevier Netherlands
Year of publication	1993
Volume	37
Issue	3-4
Supplement	0
Page range	389-395
Number of pages	7
User name	Adonis
Cost centre	Development
PCC	$20.00
Date and time	Thursday, October 09, 2003 3:25:37 PM

(FILE 'HOME' ENTERED AT 11:03:17 ON 09 OCT 2003)

FILE 'BIOSIS, LIFESCI, JAPIO, USPATFULL, EUROPATFULL, CONFSCI, MEDLINE, CAPLUS' ENTERED AT 11:03:40 ON 09 OCT 2003

L1	16	S	WESSELS, MICHAEL/AU
L2	29	S	CYWES, COLETTE/AU
L3	15		DUP REM L1 (1 DUPLICATE REMOVED)
L4	17		DUP REM L2 (12 DUPLICATES REMOVED)
L5	208274	S	STREPTOCOCCUS OR STREPTOCOCCAL
L6	15641	S	CD44
L7	1287896	S	(INHIBITS OR PREVENTS)
L8	161	S	L5 AND L6
L9	91	S	L8 AND L7
L10	91		DUP REM L9 (0 DUPLICATES REMOVED)
L11	38198	S	HYALURONIC ACID
L12	35	S	L10 AND L11

FILE 'BIOSIS, SCISEARCH, VETU, VETB, AGRICOLA' ENTERED AT 11:13:18 ON 09 OCT 2003

L13	106391	S	STREPTOCOCCUS OR STREPTOCOCCAL
L14	9197	S	CD44
L15	242438	S	(INHIBITS OR PREVENTS)
L16	11467	S	HYALURONIC ACID
L17	699	S	L16 AND L14
L18	729	S	L15 AND L13
L19	0	S	L17 AND L18
L20	23	S	L13 AND L14
L21	8	S	L20 AND L16

=>

L4 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 7

AB We used wild-type and isogenic mutant strains of group A Streptococcus (GAS) that expressed M protein, capsule, or both to study the function of M protein and the hyaluronic acid capsular polysaccharide in attachment of GAS to human keratinocytes. Types 6 and 24, but not type 18, M protein were found to mediate attachment of GAS to soft palate or skin keratinocytes, but this interaction was prevented by the hyaluronic acid capsule on highly encapsulated, or mucoid, strains. Monoclonal antibody to CD44, the principal hyaluronic acid-binding receptor on keratinocytes, inhibited attachment of both highly encapsulated and poorly encapsulated wild type strains of GAS, but not the attachment of acapsular mutants. Transfection of K562 cells with cDNA encoding human CD44 conferred the capacity to bind each of six wild-type strains of GAS, but not to bind acapsular mutants. Because, in contrast to other potential adhesins, the group A streptococcal capsule is both highly conserved and surface-exposed, it may serve as a universal adhesin for attachment of diverse strains of GAS to keratinocytes of the pharyngeal mucosa and the skin.

AN 1998:258375 BIOSIS
DN PREV199800258375

TI Hyaluronic acid capsule modulates M protein-mediated adherence and acts as a ligand for attachment of group A Streptococcus to CD44 on human keratinocytes.

AU Schrager, Harry M.; Alberti, Sebastian; **Cywes, Colette**; Dougherty, Graeme J.; Wessels, Michael R. (1)
CS (1) Channing Lab., 181 Longwood Ave., Boston, MA 02115 USA

SO Journal of Clinical Investigation, (April 15, 1998) Vol. 101, No. 8, pp. 1708-1716.
ISSN: 0021-9738.
DT Article
LA English

21 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB **CD44** is a major cell-surface receptor for **hyaluronic acid** (HA), a glycosaminoglycan component of extracellular matrix. HA-**CD44** interactions have been implicated in leukocyte extravasation into an inflammatory site. This study examined the role of **CD44** in acute inflammatory responses during pneumonias induced by Escherichia coli and **Streptococcus** pneumoniae using **CD44** -deficient mice. In E. coli-induced pneumonia, neutrophil accumulation in the lungs and edema formation was increased by 84% and 88%, respectively, in **CD44**-deficient mice compared to wild-type mice. In contrast, no difference was observed between these genotypes in S. pneumoniae-induced pneumonia, and the HA content in the lungs decreased after instillation of S. pneumoniae, but not E. coli, in both genotypes. Studies to determine the mechanisms for this enhanced response showed that: 1) neutrophil apoptosis was not different between these two genotypes in either type of pneumonia; 2) **CD44** deficiency resulted in enhanced mRNA expression of several inflammatory genes; and 3) **CD44**-deficient neutrophils migrated through Matrigel in response to chemoattractants faster and in greater numbers than wild-type neutrophils in vitro and this increase was in part dependent on HA content in the Matrigel. These data demonstrate that **CD44** deficiency results in enhanced inflammation in E. coli but not S. pneumoniae-induced pneumonia, suggesting a previously unrecognized role for **CD44** in limiting the inflammatory response to E. coli.
AN 2003:19463 BIOSIS
DN PREV200300019463
TI **CD44** deficiency leads to enhanced neutrophil migration and lung injury in Escherichia coli pneumonia in mice.
AU Wang, Qin; Teder, Priit; Judd, Nancy P.; Noble, Paul W.; Doerschuk, Claire M. (1)
CS (1) RB and C, 11100 Euclid Ave., Room 787, Cleveland, OH, 44106, USA: cmd22@po.cwru.edu USA
SO American Journal of Pathology, (December 2002, 2002) Vol. 161, No. 6, pp. 2219-2228. print.
ISSN: 0002-9440.
DT Article
LA English

L21 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB **Streptococcus** pyogenes (also known as group A **Streptococcus**, GAS), the agent of **streptococcal** sore throat and invasive soft-tissue infections, attaches to human pharyngeal or skin epithelial cells through specific recognition of its **hyaluronic acid** capsular polysaccharide by the **hyaluronic-acid**-binding protein **CD44**. Because ligation of **CD44** by **hyaluronic acid** can induce epithelial cell movement on extracellular matrix, we investigated whether molecular mimicry by the GAS **hyaluronic acid** capsule might induce similar cellular responses. Here we show that **CD44**-dependent GAS binding to polarized monolayers of human keratinocytes induced marked cytoskeletal rearrangements manifested by membrane ruffling and disruption of intercellular junctions. Transduction of the signal induced by GAS binding to **CD44** on the keratinocyte surface involved Rac1 and the cytoskeleton linker protein ezrin, as well as tyrosine phosphorylation of cellular proteins. Studies of bacterial translocation in two models of human skin indicated that cell signalling triggered by interaction of the GAS capsule with **CD44** opened intercellular junctions and promoted tissue penetration by GAS through a paracellular route. These results support a model of host cytoskeleton manipulation and tissue invasion by an extra-cellular bacterial pathogen.
AN 2002:53074 BIOSIS
DN PREV200200053074
TI Group A **Streptococcus** tissue invasion by **CD44**-mediated cell signalling.

AU Cywes, Colette; Wessels, Michael R. (1)
CS (1) Channing Laboratory, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 02115: mwessels@channing.harvard.edu USA
SO Nature (London), (6 December, 2001) Vol. 414, No. 6864, pp. 648-652. http://www.nature.com/nature/. print.
ISSN: 0028-0836.
DT Article
LA English

L21 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB The pharynx is the primary reservoir for strains of group A **Streptococcus** (GAS) associated both with pharyngitis (**streptococcal** sore throat) and with invasive or "flesh-eating" soft tissue infections. We now report that **CD44**, a **hyaluronic acid**-binding protein that mediates human cell-cell- and cell-extracellular matrix-binding interactions, functions as a receptor for GAS colonization of the pharynx in vivo. We found that attachment of GAS to murine epithelial keratinocytes was mediated by binding of the GAS **hyaluronic acid** capsular polysaccharide to **CD44**. In studies of transgenic mice with a selective defect in epithelial expression of **CD44**, GAS adherence to **CD44**-deficient keratinocytes in vitro was reduced compared with adherence to keratinocytes expressing normal levels of **CD44** . After intranasal inoculation, GAS colonized the oropharynx of wild-type mice but failed to colonize transgenic mice deficient in **CD44** expression. GAS colonization of wild-type mice could be blocked by coadministration of mAb to **CD44** or by pretreatment of the animals with exogenous **hyaluronic acid**. These results provide evidence that **CD44** serves as a receptor for GAS colonization of the pharynx and support the potential efficacy of disrupting the interaction between the GAS **hyaluronic acid** capsule and **CD44** as a novel approach to preventing pharyngeal infection.
AN 2000:524546 BIOSIS
DN PREV200000524546
TI **CD44** as a receptor for colonization of the pharynx by group A **Streptococcus**.
AU Cywes, Colette; Stamenkovic, Ivan; Wessels, Michael R. (1)
CS (1) Channing Laboratory, 181 Longwood Avenue, Boston, MA, 02115 USA
SO Journal of Clinical Investigation, (October, 2000) Vol. 106, No. 8, pp. 995-1002. print.
ISSN: 0021-9738.
DT Article
LA English
SL English

L21 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB We used wild-type and isogenic mutant strains of group A **Streptococcus** (GAS) that expressed M protein, capsule, or both to study the function of M protein and the **hyaluronic acid** capsular polysaccharide in attachment of GAS to human keratinocytes. Types 6 and 24, but not type 18, M protein were found to mediate attachment of GAS to soft palate or skin keratinocytes, but this interaction was prevented by the **hyaluronic acid** capsule on highly encapsulated, or mucoid, strains. Monoclonal antibody to **CD44**, the principal **hyaluronic acid**-binding receptor on keratinocytes, inhibited attachment of both highly encapsulated and poorly encapsulated wild type strains of GAS, but not the attachment of acapsular mutants. Transfection of K562 cells with cDNA encoding human **CD44** conferred the capacity to bind each of six wild-type strains of GAS, but not to bind acapsular mutants. Because, in contrast to other potential adhesins, the group A **streptococcal** capsule is both highly conserved and surface-exposed, it may serve as a universal adhesin for attachment of diverse strains of GAS to keratinocytes of the pharyngeal

mucosa and the skin.
AN 1998:258375 BIOSIS
DN PREV199800258375
TI **Hyaluronic acid** capsule modulates M protein-mediated adherence and acts as a ligand for attachment of group A **Streptococcus** to **CD44** on human keratinocytes.
AU Schrager, Harry M.; Alberti, Sebastian; Cywes, Colette; Dougherty, Graeme J.; Wessels, Michael R. (1)
CS (1) Channing Lab., 181 Longwood Ave., Boston, MA 02115 USA
SO Journal of Clinical Investigation, (April 15, 1998) Vol. 101, No. 8, pp. 1708-1716.
ISSN: 0021-9738.
DT Article
LA English

L21 ANSWER 5 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB **CD44** is a major cell-surface receptor for **hyaluronic acid** (HA), a glycosaminoglycan component of extracellular matrix. HA-**CD44** interactions have been implicated in leukocyte extravasation into an inflammatory site. This study examined the role of **CD44** in acute inflammatory responses during pneumonias induced by Escherichia coli and **Streptococcus** pneumoniae using **CD44** -deficient mice. In E. coli-induced pneumonia, neutrophil accumulation in the lungs and edema formation was increased by 84% and 88%, respectively, in **CD44**-deficient mice compared to wild-type mice. In contrast, no difference was observed between these genotypes in S. pneumoniae-induced pneumonia, and the RA content in the lungs decreased after instillation of S. pneumoniae, but not E coli, in both genotypes. Studies to determine the mechanisms for this enhanced response showed that: 1) neutrophil apoptosis was not different between these two genotypes in either type of pneumonia; 2) **CD44** deficiency resulted in enhanced mRNA expression of several inflammatory genes; and 3) **CD44**-deficient neutrophils migrated through Matrigel in response to chemoattractants faster and in greater numbers than wild-type neutrophils in vitro and this increase was in part dependent on HA content in the Matrigel. These data demonstrate that **CD44** deficiency results in enhanced inflammation in E. coli but not S. pneumoniae-induced pneumonia, suggesting a previously unrecognized role for **CD44** in limiting the inflammatory response to E. coli.
AN 2003:1040 SCISEARCH
GA The Genuine Article (R) Number: 622TP
TI **CD44** deficiency leads to enhanced neutrophil migration and lung injury in Escherichia coli pneumonia in mice
AU Wang Q; Teder P; Judd N P; Noble P W; Doerschuk C M (Reprint)
CS Room 787, 111000 Euclid Ave, RB&C, Cleveland, OH 44106 USA (Reprint); Vet Adm Connecticut Healthcare Syst, West Haven, CT USA; Yale Univ, Sch Med, Pulm & Crit Care Sect, West Haven, CT 06516 USA; Case Western Reserve Univ, Cleveland, OH 44106 USA; Rainbow Babies & Childrens Hosp, Dept Pediat, Div Integrat Biol, Cleveland, OH 44106 USA
CYA USA
SO AMERICAN JOURNAL OF PATHOLOGY, (DEC 2002) Vol. 161, No. 6, pp. 2219-2228.
Publisher: AMER SOC INVESTIGATIVE PATHOLOGY, INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3993 USA.
ISSN: 0002-9440.
DT Article; Journal
LA English
REC Reference Count: 54
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 6 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB **Streptococcus** pyogenes (also known as group A **Streptococcus**, GAS), the agent of **streptococcal** sore throat and invasive soft-tissue infections, attaches to human pharyngeal or skin epithelial cells through specific recognition of its

hyaluronic acid capsular polysaccharide by the **hyaluronic-acid**-binding protein **CD44** (refs 1, 2). Because ligation of **CD44** by **hyaluronic acid** can induce epithelial cell movement on extracellular matrix(3-5), we investigated whether molecular mimicry by the GAS **hyaluronic acid** capsule might induce similar cellular responses. Here we show that **CD44**-dependent GAS binding to polarized monolayers of human keratinocytes induced marked cytoskeletal rearrangements manifested by membrane ruffling and disruption of intercellular junctions. Transduction of the signal induced by GAS binding to **CD44** on the keratinocyte surface involved Rac1 and the cytoskeleton linker protein ezrin, as well as tyrosine phosphorylation of cellular proteins. Studies of bacterial translocation in two models of human skin indicated that cell signalling triggered by interaction of the GAS capsule with **CD44** opened intercellular junctions and promoted tissue penetration by GAS through a paracellular route. These results support a model of host cytoskeleton manipulation and tissue invasion by an extracellular bacterial pathogen.

AN 2001:965709 SCISEARCH
GA The Genuine Article (R) Number: 498WB
TI Group A **Streptococcus** tissue invasion by **CD44**-mediated cell signalling
AU Cywes C; Wessels M R (Reprint)
CS Harvard Univ, Sch Med, Brigham & Womens Hosp, Channing Lab, Boston, MA 02115 USA (Reprint); Harvard Univ, Sch Med, Childrens Hosp, Div Infect Dis, Boston, MA 02115 USA
CYA USA
SO NATURE, (6 DEC 2001) Vol. 414, No. 6864, pp. 648-652.
Publisher: MACMILLAN PUBLISHERS LTD, PORTERS SOUTH, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
ISSN: 0028-0836.
DT Article; Journal
LA English
REC Reference Count: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 7 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB The pharynx is the primary reservoir for strains of group A **Streptococcus** (GAS) associated both with pharyngitis (**streptococcal** sore throat) and with invasive or ''flesh-eating'' soft tissue infections. We now report that **CD44**, a **hyaluronic acid**-binding protein that mediates human cell-cell- and cell-extracellular matrix-binding interactions, functions as a receptor for GAS colonization of the pharynx in vivo. We found that attachment of GAS to murine epithelial keratinocytes was mediated by binding of the GAS **hyaluronic acid** capsular polysaccharide to **CD44**. In studies of transgenic mice with a selective defect in epithelial. expression of **CD44**, GAS adherence to **CD44**-deficient keratinocytes in vitro was reduced compared with adherence to keratinocytes expressing normal levels of **CD44**. After intranasal inoculation, GAS colonized the oropharynx of wild-type mice but failed to colonize transgenic mice deficient in **CD44** expression. GAS colonization of wild-type mice could be blocked by coadministration of mAb to **CD44** or by pretreatment of the animals with exogenous **hyaluronic acid**. These results provide evidence that **CD44** serves as a receptor for GAS colonization of the pharynx and support the potential efficacy of disrupting the interaction between the GAS **hyaluronic acid** capsule and **CD44** as a novel approach to preventing pharyngeal infection.

AN 2000:796713 SCISEARCH
GA The Genuine Article (R) Number: 364XQ
TI **CD44** as a receptor for colonization of the pharynx by group A **Streptococcus**

AU Cywes C; Stamenkovic I; Wessels M R (Reprint)
CS BRIGHAM & WOMENS HOSP, CHANNING LAB, 181 LONGWOOD AVE, BOSTON, MA 02115 (Reprint); BRIGHAM & WOMENS HOSP, CHANNING LAB, BOSTON, MA 02115; BRIGHAM & WOMENS HOSP, DIV INFECT DIS, BOSTON, MA 02115; MASSACHUSETTS GEN HOSP, BOSTON, MA; HARVARD UNIV, SCH MED, DEPT PATHOL, BOSTON, MA 02115; HARVARD UNIV, SCH MED, DEPT MED, BOSTON, MA 02115
CYA USA
SO JOURNAL OF CLINICAL INVESTIGATION, (OCT 2000) Vol. 106, No. 8, pp. 995-1002.
Publisher: AMER SOC CLINICAL INVESTIGATION INC, ROOM 4570 KRESGE I, 200 ZINA PITCHER PLACE, ANN ARBOR, MI 48109-0560.
ISSN: 0021-9738.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 39
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 8 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB We used wild-type and isogenic mutant strains of group A **Streptococcus** (GAS) that expressed M protein, capsule, or both to study the function of M protein and the **hyaluronic acid** capsular polysaccharide in attachment of GAS to human keratinocytes. Types 6 and 24, but not type 18, M protein tt ere found to mediate attachment of GAS to soft palate or skin keratinocytes, but this interaction was prevented by the **hyaluronic acid** capsule on highly encapsulated, or mucoid, strains, Monoclonal antibody to **CD44**, the principal **hyaluronic acid**-binding receptor on keratinocytes, inhibited attachment of both highly encapsulated and poorly encapsulated wild type strains of GAS, but not the attachment of acapsular mutants, Transfection of K562 cells with cDNA encoding human **CD44** conferred the capacity to bind each of six wild-type strains of GAS, but not to bind acapsular mutants. Because, in contrast to other potential adhesins. the group A **streptococcal** capsule is both highly conserved and surface-exposed, it may serve as a universal adhesin for attachment of diverse strains of GAS to keratinocytes of the pharyngeal mucosa and the skin.
AN 1998:323631 SCISEARCH
GA The Genuine Article (R) Number: ZJ234
TI **Hyaluronic acid** capsule modulates M protein-mediated adherence and acts as a ligand for attachment of group A **Streptococcus** to **CD44** on human keratinocytes
AU Schrager H M; Alberti S; Cywes C; Dougherty G J; Wessels M R (Reprint)
CS BRIGHAM & WOMENS HOSP, CHANNING LAB, 181 LONGWOOD AVE, BOSTON, MA 02115 (Reprint); BRIGHAM & WOMENS HOSP, CHANNING LAB, BOSTON, MA 02115; HARVARD UNIV, BETH ISRAEL DEACONESS MED CTR, SCH MED, DIV INFECT DIS, BOSTON, MA 02115; BRITISH COLUMBIA CANC RES CTR, TERRY FOX LAB, VANCOUVER, BC V5Z 1L3, CANADA
CYA USA; CANADA
SO JOURNAL OF CLINICAL INVESTIGATION, (15 APR 1998) Vol. 101, No. 8, pp. 1708-1716.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021.
ISSN: 0021-9738.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 41
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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(FILE 'HOME' ENTERED AT 13:26:21 ON 09 OCT 2003)

FILE 'BIOSIS, SCISEARCH, VETU, VETB, AGRICOLA' ENTERED AT 13:28:25 ON 09 OCT 2003

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L1         11467 S HYALURONIC ACID
L2       2633852 S (INHIBIT? OR PREVENT?)
L3        106391 S STREPTOCOCCAL OR STREPTOCOCCUS
L4           865 S L1 AND (INJECT? OR VACCINAT? OR ADMINISTER? OR IMMUNIZ?)
L5            24 S L4 AND L3
L6            24 S L5 AND L3
L7            19 DUP REM L6 (5 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1

AB Acute rheumatic fever is a serious autoimmune sequel of **Streptococcus** pyogenes infection. This study shows that serotype M3 and M18 S. pyogenes isolated during outbreaks of rheumatic fever have the unique capability to bind and aggregate human basement membrane collagen type IV. M3 protein is identified as collagen-binding factor of M3 streptococci, whereas M18 isolates bind collagen through a **hyaluronic acid** capsule, revealing a novel function for M3 protein and capsule. Following in vivo mouse passage, conversion of a nonencapsulated and collagen-binding negative M1 S. pyogenes into an encapsulated, collagen-binding strain further supports the crucial role of capsule in mediating collagen binding. Collagen binding represents a novel colonization mechanism, as it is demonstrated that S. pyogenes bind to collagen matrix in vitro and in vivo. Moreover, **immunization** of mice with purified recombinant M3 protein led to the generation of anti-collagen type IV antibodies. Finally, sera from acute rheumatic fever patients had significantly increased titers of anti-collagen type IV antibodies as compared with healthy controls. These findings may suggest a link between the potential of rheumatogenic S. pyogenes isolates to bind collagen, and the presence of collagen-reactive autoantibodies in the serum of rheumatic fever patients, which may form a basis for post-**streptococcal** rheumatic disease. These anti-collagen antibodies may form a basis for poststreptococcal rheumatic disease.

AN 2003:324236 BIOSIS

DN PREV200300324236

TI Rheumatic fever-associated **Streptococcus** pyogenes isolates aggregate collagen.

AU Dinkla, Katrin; Rohde, Manfred; Jansen, Wouter T. M.; Kaplan, Edward L.; Chhatwal, Gursharan S.; Talay, Susanne R. (1)

CS (1) Department of Microbial Pathogenesis and Vaccine Research, GBF-German Research Centre for Biotechnology, 38124, Braunschweig, Germany: sta@gbf.de Germany

SO Journal of Clinical Investigation, (June 2003, 2003) Vol. 111, No. 12, pp. 1905-1912. print.
ISSN: 0021-9738.

DT Article

LA English

L7 ANSWER 2 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB The frequency at which the genes responsible for capsule biosynthesis occurred in field isolates of **Streptococcus** uberis was determined. Of the two genotypes detected (hasABC and hasC), the capsular genotype (hasABC) was more common. This genotype was present at a higher frequency in a population isolated from mastitis cases than in a population isolated from cattle bedding. The virulence of a mutant strain of S. uberis (TRE0-6) that lacked the ability to produce a **hyaluronic acid** capsule due to an insertion within its single copy of hasA (P. N. Ward, T. R. Field, W. G. F. Ditcham, E. Maguin, and J. A. Leigh, Infect. Immun. 69:392-399, 2001) was compared to that of the capsular parental strain (0140J). Strains TRFO-6 and 0140J infected all mammary gland quarters following experimental challenge. The wild type and the mutant induced overt signs of disease in four out of four and in six out of eight mammary gland quarters, respectively. Both the wild type and the hasA mutant were resistant to killing by bovine neutrophils following cultivation in bovine milk. The ability to withstand the bactericidal action of neutrophils following growth in milk was therefore independent of the capsule and coincided with the ability of supernatants from such cultures to prevent the bactericidal action of neutrophils. This investigation revealed that, in the absence of the capsule, S. uberis is able to withstand the bactericidal effect of bovine neutrophils and induce mastitis in dairy cows.

AN 2003:75897 SCISEARCH

GA The Genuine Article (R) Number: 632EZ

TI The **hyaluronic acid** capsule of **Streptococcus** uberis is not required for the development of infection and clinical mastitis
AU Field T R; Ward P N; Pedersen L H; Leigh J A (Reprint)
CS Inst Anim Hlth, Compton Lab, Newbury RG20 7NN, Berks, England (Reprint); Royal Vet & Agr Univ, Inst Vet Microbiol, DK-1870 Frederiksberg C, Denmark
CYA England; Denmark
SO INFECTION AND IMMUNITY, (JAN 2003) Vol. 71, No. 1, pp. 132-139. Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.
DT Article; Journal
LA English
REC Reference Count: 28
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 3 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2
AB Background/Aims: Activation of reticuloendothelial system functions by the treatment with OK-432 has been reported to enhance liver regeneration. However, its effect on liver regeneration has not been studied after hepatectomy under ischemia/reperfusion which is in clinical use. The aim was to examine the effect of OK-432 on regeneration and energy status of the liver after hepatectomy under ischemia/reperfusion in rats. Methodology: Rats were randomly divided into two groups; OK-432 pretreatment and saline treatment (control) group. In the OK-432 group, OK-432 (2.5mg/kg body weight) was **administered** intraperitoneally 24 hours before hepatectomy. In the control group, the same volume of physiological saline was **administered** in the same manner. Seventy percent hepatectomy was performed in both groups during the second 15-minute ischemia period after an initial 15-minute ischemia and 15-minute reperfusion periods. The survival after hepatectomy, relative liver weight, deoxyribonucleic acid synthesis rate, and hepatic adenine nucleotide and energy charge levels were examined immediately after hepatectomy and on postoperative days 1, 2, 3, and 7. Serum levels of total bilirubin, glutamic pyruvic transaminase, and **hyaluronic acid** were also measured. Results: All rats survived and the relative liver weight and deoxyribonucleic acid synthesis rate were not significantly different in the two groups. Serum total bilirubin and glutamic pyruvic transaminase levels were not significantly different in both groups. The serum concentration of **hyaluronic acid** immediately after hepatectomy was significantly higher in the OK-432 group than in the control group. The pretreatment with OK-432 had no significant effect on the levels of adenine nucleotides and energy charge in the liver. Conclusions: Under ischemia/reperfusion, pretreatment with OK-432 has no significant effect on regeneration and energy status of the liver after hepatectomy.
AN 2002:273052 BIOSIS
DN PREV200200273052
TI Effects of **streptococcal** preparation OK-432 on liver regeneration and energy status after partial hepatectomy under ischemia/reperfusion in rats.
AU Watanabe, Masato; Chijiiwa, Kazuo (1); Kameoka, Nobuhisa; Nakano, Kenji; Noshiro, Hirokazu; Tanaka, Masao
CS (1) Hepatobiliary and Pancreatic Surgery, Department of Surgery and Oncology, Kyushu University Graduate School of Medicine, Fukuoka, 812-8582 Japan
SO Hepato-Gastroenterology, (January February, 2002) Vol. 49, No. 43, pp. 218-221. print.
ISSN: 0172-6390.
DT Article
LA English

L7 ANSWER 4 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB Group A **streptococcus** (GAS) causes diseases ranging from benign to severe infections such as necrotizing fasciitis (NF). The reasons for the differences in severity of **streptococcal** infections are unexplained. We developed the polymorphic-tag-lengths-transposon-mutagenesis (PTTM) method to identify virulence genes in vivo. We applied PTTM on an emm14 strain isolated from a patient with NF and screened for mutants of decreased virulence, using a mouse model of human soft-tissue infection. A mutant that survived in the skin but was attenuated in its ability to reach the spleen and to cause a lethal infection was identified. The transposon was inserted into a small open reading frame (ORF) in a locus termed sil, **streptococcal** invasion locus. sil contains at least five genes (silA-E) and is highly homologous to the quorum-sensing competence regulons of **Streptococcus** pneumoniae. silA and sil B encode a putative two-component system whereas silD and silE encode two putative ABC transporters. silC is a small ORF of unknown function preceded by a combox promoter. Insertion and deletion mutants of sil had a diminished lethality in the animal model. Virulence of a deletion mutant of silC was restored when **injected** together with the avirulent emm14-deletion mutant, but not when these mutants were **injected** into opposite flanks of a mouse. DNA transfer between these mutants occurred in vivo but could not account for the complementation of virulence. DNA exchange between the emm14-deletion mutant and mutants of sil occurred also in vitro, at a frequency of similar to 10(-8) for a single antibiotic marker. Whereas silC and silD mutants exchanged markers with the emm14 mutant, silB mutant did not. Thus, we identified a novel locus, which controls GAS spreading into deeper tissues and could be involved in DNA transfer.
AN 2002:840170 SCISEARCH
GA The Genuine Article (R) Number: 600CG
TI A locus of group A **streptococcus** involved in invasive disease and DNA transfer
AU Hidalgo-Grass C; Ravins M; Dan-Goor M; Jaffe J; Moses A E; Hanski E (Reprint)
CS Hebrew Univ Jerusalem, Hadassah Med Sch, Dept Clin Microbiol, IL-91120 Jerusalem, Israel (Reprint); Hadassah Univ Hosp, Dept Clin Microbiol & Infect Dis, IL-91120 Jerusalem, Israel
CYA Israel
SO MOLECULAR MICROBIOLOGY, (OCT 2002) Vol. 46, No. 1, pp. 87-99.
Publisher: BLACKWELL PUBLISHING LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0950-382X.
DT Article; Journal
LA English
REC Reference Count: 52
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 5 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB Background: IL-1Ra is a promising agent in the treatment of rheumatoid arthritis. However, earlier work, using IL-1R knockout mice, showed an important role for IL-1 in the innate immune response against lung infections. Aims and Methods: We investigated the influence of IL-1R blockade by IL-1Ra (10mg/kg), **administered** in **hyaluronic acid** to prolong half life (0 and 24h), and the influence of genetic background, on host defense and mortality in mice during S. pneumoniae pneumonia. Cytokines chemokines (ELISA), MPO and CFU were measured in lung homogenates of BALBc and C57BL/6 mice. Statistics by Mann-Whitney. Results: Survival did not differ between IL-1Ra and vehicle (Veh) treated mice. However, at early time points (24 and 48h), IL-1Ra treated BALBc mice had more S. pneumoniae CFU in lungs than Veh treated mice ($P<0.005$). C57BL/6 mice treated with IL-1Ra had more CFU in the lungs after 24h, but an equal number of pneumococci in the lungs after 48h. Cytokine (TNF) and chemokine (MIP-1a, MIP-2) concentrations were similar in IL-1Ra and Veh treated mice at 24 and 48h in both strains. MPO content of lungs showed no differences either. Conclusion: Although IL-1Ra

treatment impaired antibacterial defense during the early phase of pneumococcal pneumonia, this influence was transient and did not result in an enhanced mortality. This finding was unrelated to the genetic background of the mice.

AN 2003:277882 BIOSIS
DN PREV200300277882
TI Treatment with recombinant IL-1 receptor antagonist (IL-1Ra) only transiently impairs antibacterial defense against murine pneumococcal pneumonia.
AU Rijneveld, A. W. (1); Florquin, S.; Speelman, P.; Edwards, C. K.; Dinarello, C. A.; van der Poll, T. (1)
CS (1) Lab. of Exp. Int. Med., Acad. Med. Ctr., Amsterdam, Netherlands Netherlands
SO Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 40-41. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, CA, USA September 27-30, 2002 American Society for Microbiology
.
DT Conference
LA English

L7 ANSWER 6 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB Nasopharyngeal colonization is a necessary first step in the pathogenesis of **Streptococcus** pneumoniae. Using isolates containing defined mutations in the S. pneumoniae capsule locus, we found that expression of the capsular polysaccharide is essential for colonization by the type 2 strain D39 and the type 3 strains A66 and WU2. Nonencapsulated derivatives of each of these strains were unable to colonize BALB/cByJ mice. Similarly, type 3 mutants that produced <6% of the parental amounts of capsule could not colonize. Capsule production equivalent to that of the parent strain was not required for efficient colonization, however, as type 3 mutants producing approximately 20% of the parental amounts of capsule colonized as effectively as the parent. This 80% reduction in capsule level had only a minimal effect on intraperitoneal virulence but caused a significant reduction in virulence via the intravenous route. In the X-linked immunodeficient CBA/N mouse, the type 3 mutant producing similar to 20% of the parental amount of capsule (AM188) was diminished in its ability to cause invasive disease and death following intranasal inoculation. Following intravenous or intraperitoneal challenge, however, only extended survival times were observed. Our results demonstrate an additional role for capsule in the pathogenesis of S. pneumoniae and show that isolates producing reduced levels of capsule can remain highly virulent.

AN 2001:427263 SCISEARCH
GA The Genuine Article (R) Number: 433WU
TI Requirement for capsule in colonization by **Streptococcus** pneumoniae
AU Magee A D; Yother J (Reprint)
CS Univ Alabama, Dept Microbiol, BBRB 661-12, 845 19th St S, Birmingham, AL 35294 USA (Reprint); Univ Alabama, Dept Microbiol, Birmingham, AL 35294 USA
CYA USA
SO INFECTION AND IMMUNITY, (JUN 2001) Vol. 69, No. 6, pp. 3755-3761.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.
DT Article; Journal
LA English
REC Reference Count: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 7 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3

AB A symptomatic relief by **hyaluronic acid** (HA, MW: 3.5X106), which is synthesized by **Streptococcus** spp, was investigated in experimental ovine osteoarthrosis. Bilateral osteoarthrosis (OA) of the temporo-mandibular joints (TMJs) was induced by perforating discs and by scrapping subchondral condylar surface. HA was intra-articularly **injected** into the left joints of 6 sheep on 7, 10, 14, 17 and 21 days after the operation and physiological saline as the control was **injected** into the contralateral (right) joints on the same day. Three sheep were killed at 1 month post-operation (MPO) and the remaining three sheep were killed at 3 MPO. Various responses such as proliferation of fibrous tissue, denudation, erosion, osteophyte formation, subcortical cyst formation and ankylosis were observed radiographically and histopathologically. The treatment of HA ameliorated the degenerative changes and lowered the osteoarthrotic score in the left joints at 1 MPO (9.96 vs 5.81) and 3 MPO (10.86 vs 5.29) compared to the right joints. These results indicate that a repeated intra-articular **injection** of HA inhibits the progression of OA in ovine TMJs by inducing the development of articular cartilage and by reducing the proliferation of fibrotic tissue.
AN 2001:573626 BIOSIS
DN PREV200100573626
TI Therapeutic effect of **hyaluronic acid** on experimental osteoarthrosis of ovine temporomandibular joint.
AU Kim, Chang-Hwan; Lee, Beom-Jun; Yoon, Junghee; Seo, Kang-Moon; Park, Jong-Hwan; Lee, Jin-Won; Choi, Eun-Sil; Hong, Jung-Ju; Lee, Yong-Soon; Park, Jae-Hak (1)
CS (1) Department of Laboratory Animal Medicine, College of Veterinary Medicine, Seoul National University, 103 Seodun-dong, Kwonsun-gu, Suwon, 441-744 South Korea
SO Journal of Veterinary Medical Science, (October, 2001) Vol. 63, No. 10, pp. 1083-1089. print.
ISSN: 0916-7250.
DT Article
LA English
SL English

L7 ANSWER 8 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
AB JRS4(HE), a highly encapsulated, mouse-passaged variant of group A **streptococcal** strain JRS4, was characterized. The mucoid phenotype of JRS4(HE) was preserved after extensive passage in vitro. The level and size of csrRS transcript in JRS4(HE) was similar to that of JRS4, yet JRS4(HE) expressed high levels of has and sagA and exhibited an increased activity of streptolysin S. These findings indicate that the CsrRS repressor system was inactive in JRS4(HE). JRS4(HE) adhered to HEp-2 cells at the stationary phase but did not internalize these cells. At midlogarithmic phase, JRS4(HE) neither adhered to nor internalized cells, because of an increased amount of **hyaluronic acid**.
Mice **injected** subcutaneously with JRS4(HE) developed large, deep necrotic lesions. In contrast, mice challenged with JRS4 developed small, superficial lesions. Despite the use of a high inoculum, mice challenged with JRS4(HE) did not develop a lethal bacteremic infection. It is concluded that inactivation of CsrRS in vivo is insufficient to cause a spreading necrotic disease.
AN 2001:12441 BIOSIS
DN PREV200100012441
TI Characterization of a mouse-passaged, highly encapsulated variant of group A **streptococcus** in in vitro and in vivo studies.
AU Ravins, Miriam; Jaffe, Joseph; Hanski, Emanuel (1); Shetzigovski, Ilanit; Natanson-Yaron, Shira; Moses, Allon E.
CS (1) Dept. of Clinical Microbiology, Hebrew University-Hadassah Medical School, Jerusalem, 91010: hanski@cc.huji.ac.il Israel
SO Journal of Infectious Diseases, (December, 2000) Vol. 182, No. 6, pp. 1702-1711. print.

ISSN: 0022-1899.
DT Article
LA English
SL English

L7 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5
AB Passage in human blood of group A **streptococcal** isolate 64p was previously shown to result in the enhanced expression of M and M-related proteins. Similarly, when this isolate was **injected** into mice via an air sac model for skin infection, organisms recovered from the spleens showed both increased expression of M and M-related proteins and increased skin-invasive potential. We show that these phenotypic changes were not solely the result of increased transcription of the mRNAs encoding the M and M-related gene products. Rather, the altered expression was associated with posttranslational modifications of the M and M-related proteins that occur in this strain, based on the presence or absence of another virulence protein, the **streptococcal** cysteine protease SpeB. The phenotypic variability also correlates with colony size variation. Large colonies selected by both regimens expressed more **hyaluronic acid**, which may explain differences in colony morphology. All large-colony variants were SpeB negative and expressed three distinct immunoglobulin G (IgG)-binding proteins in the M and M-related protein family. Small-colony variants were SpeB positive and bound little IgG through their M and M-related proteins because these proteins, although made, were degraded or altered in profile by the SpeB protease. We conclude that passage in either human blood or a mouse selects for a stable, phase-varied strain of group A streptococci which is altered in many virulence properties.
AN 2000:106310 BIOSIS
DN PREV200000106310
TI Absence of SpeB production in virulent large capsular forms of group A **streptococcal** strain 64.
AU Raeder, Roberta; Harokopakis, Evlambia; Hollingshead, Susan; Boyle, Michael D. (1)
CS (1) Department of Microbiology and Immunology, Medical College of Ohio, 3055 Arlington Ave., Toledo, OH, 43613-5806 USA
SO Infection and Immunity, (Feb., 2000) Vol. 68, No. 2, pp. 744-751. ISSN: 0019-9567.
DT Article
LA English
SL English

L7 ANSWER 10 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB **Hyaluronic acid** (HA) derivatives have been developed to try to enhance rheological properties of this molecule to make it suitable for various medical applications. The main dermatological application of HA derivatives is the augmentation of soft tissues, via **injection** into the dermis. HA derivatives are indicated for the correction of cutaneous contour deficiencies of the skin, particularly in cases of ageing or degenerative lesions or to increase lips. Two HA derivatives have been evaluated: Hylaform(R) Viscoelastic Gel (Hylan B), derived from rooster combs and subjected to cross-linking, and Restylane(R), produced through bacterial fermentation (streptococci) and stabilized, as declared by the producer. In both cases the purpose is to improve HA rheological characteristics and slow down its degradation once it is in contact with biological structures. Distribution of particle dimensions, pH, protein concentration and rheological properties have been investigated in order to evaluate their reliability as fillers for soft tissue augmentation. The results of the analyses showed that there are differences between Rest ylane(R) and Hylaform(R). Especially as far as rheological characteristics are concerned, the results outline different structures of the products: Hylaform(R) behaves as a strong hydrogel, Restylane(R) as a weak hydrogel; theologically Hylaform(R) is clearly

superior to Restylane(R). Hylaform(R) contains a definitely minor quantity (about a quarter) of cross-linked **hyaluronic acid** than Restylane(R). Furthermore, although not declared by the manufacturer, Restylane(R) contains protein, resulting from bacterial fermentation or added to enable cross-linking reaction; the quantity of proteins contained by Restylane(R) can be as much as four times the quantity contained by Hylaform(R), for the same volume (1 ml). It is evident that Hylaform(R) offers higher safety margin than Restylane(R). Furthermore, wide literature and 20 years of clinical experience on hyaluronan derived from rooster combs confirm the reliability of this derivative while we did not find evidence regarding about the safety of HA obtained from **streptococcus**.

AN 2000:74144 SCISEARCH
GA The Genuine Article (R) Number: 275VJ
TI Comparative chemical evaluation of two commercially available derivatives of **hyaluronic acid** (Hylaform((R)) from rooster combs and Restylane((R)) from **streptococcus**) used for soft tissue augmentation
AU Manna F (Reprint); Dentini M; Desideri P; DePita O; Mortilla E; Maras B
CS UNIV ROMA LA SAPIENZA, DEPT CHEM & TECHNOL STUDIES BIOLOGICALLY ACT SUBS, PIAZZALE ALDO MORO 5, I-00185 ROME, ITALY (Reprint); UNIV ROMA LA SAPIENZA, DEPT CHEM, I-00185 ROME, ITALY; IRCCS, IDI, ROME, ITALY; CONSORZIO UNIV, LABTEGNOS, REGGIO CALABRIA, ITALY; UNIV ROMA LA SAPIENZA, DEPT BIOCHEM SCI A ROSSI FANELLI, ROME, ITALY
CYA ITALY
SO JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY, (NOV 1999) Vol. 13, No. 3, pp. 183-192.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0926-9959.
DT Article; Journal
FS CLIN
LA English
REC Reference Count: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 11 OF 19 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. (2003) on STN
AN 1999:69469 AGRICOLA
DN IND22007587
TI Recombinant hyaluronate associated protein as a protective immunogen against **Streptococcus** equi and **Streptococcus** zooepidemicus challenge in mice.
AU Chanter, N.; Ward, C.L.; Talbot, N.C.; Flanagan, J.A.; Binns, M.; Houghton, S.B.; Smith, K.C.; Mumford, J.A.
CS Animal Health Trust, Suffolk, UK.
AV DNAL (QR175.M53)
SO Microbial pathogenesis, Sept 1999. Vol. 27, No. 3. p. 133-143
Publisher: London ; Orlando : Academic Press, c1986-
CODEN: MIPAEV; ISSN: 0882-4010
NTE Includes references
CY England; United Kingdom
DT Article
FS Non-U.S. Imprint other than FAO
LA English

L7 ANSWER 12 OF 19 SCISEARCH
AB Group A streptococci (GAS) are responsible for numerous human illnesses, ranging from pharyngitis to severe invasive infections, such as necrotizing fascitis and toxic shock syndrome to the postinfectious sequelae, acute rheumatic fever (ARF), and glomerulonephritis. To date, to develop a vaccine, studies have focused on the M protein. However,

designing a vaccine to prevent GAS infection based on this molecule has been hampered by the vast number of M protein serotypes and the possibility that it may induce potentially harmful autoimmune reactions. In this article, the authors discuss recent approaches to overcoming the problems of an M protein-based vaccine. In addition, recent studies identifying the protective properties of other **streptococcal** antigens and their potential as vaccine candidates are discussed.

AN 1999:366282 SCISEARCH
GA The Genuine Article (R) Number: 193CN
TI Vaccine strategies to prevent rheumatic fever
AU Brandt E R (Reprint); Good M F
CS POB ROYAL BRISBANE HOSP, BRISBANE, QLD 4029, AUSTRALIA (Reprint); QUEENSLAND INST MED RES, COOPERAT CTR VACCINE TECHNOL, MOL IMMUNOL LAB, BRISBANE, QLD 4006, AUSTRALIA
CYA AUSTRALIA
SO IMMUNOLOGIC RESEARCH, (10 APR 1999) Vol. 19, No. 1, pp. 89-103. Publisher: HUMANA PRESS INC, 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512.
ISSN: 0257-277X.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 82
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 13 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB Resistance to phagocytosis is a hallmark of virulent **Streptococcus** pyogenes (group A **streptococcus**), Surface bound C5a peptidase reduces recruitment of phagocytes to the site of infection, and **hyaluronic acid** capsules and/or the M protein limit the uptake of streptococci, In this study the relative impact of M and M-like proteins and the C5a peptidase on the virulence of a serotype M49 strain was assessed. The capacities of isogenic strains with an insertion mutation in emm49; with a deletion mutation in scpA49 (C5a peptidase gene); and,vith a deletion that removes all three M-like genes, mrp49, emm49, and enn49, to colonize mice and resist phagocytosis were compared. Experiments confirmed results obtained in an earlier study, which showed that the M49 protein was not required for in vitro resistance to phagocytosis, and also showed that the M protein was not required for colonization of mice. Failure to produce all three M-like proteins, M49, Mrp, and Enn49, significantly reduced the ability of these streptococci to resist phagocytosis in vitro but did not significantly alter the persistence of streptococci on the oral mucosa, In vitro experiments indicate that M+ streptococci are phagocytized by polymorphonuclear leukocytes that have been activated with phorbol-12-myristate 13-acetate or recombinant human C5a, This observation may explain the finding that expression of M49 protein is not essential for short-term colonization of the mouse oral mucosa.

AN 1998:832107 SCISEARCH
GA The Genuine Article (R) Number: 132HT
TI Impact of M49, mrp, enn, and C5a peptidase proteins on colonization of the mouse oral mucose by **Streptococcus** pyogenes
AU Ji Y D; Schnitzler N; DeMaster E; Cleary P (Reprint)
CS UNIV MINNESOTA, DEPT MICROBIOL, BOX 196 FUMC, MINNEAPOLIS, MN 55455 (Reprint); UNIV MINNESOTA, DEPT MICROBIOL, MINNEAPOLIS, MN 55455; UNIV HOSP AACHEN, NATL REFERENCE LAB STREPTOCOCCI, AACHEN, GERMANY; UNIV HOSP AACHEN, INST MED MICROBIOL, AACHEN, GERMANY
CYA USA; GERMANY
SO INFECTION AND IMMUNITY, (NOV 1998) Vol. 66, No. 11, pp. 5399-5405. Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DT Article; Journal
FS LIFE

LA English
REC Reference Count: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 14 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB **Streptococcal** pyrogenic exotoxin B (SpeB), a conserved cysteine protease expressed by virtually all **Streptococcus** pyogenes strains, has recently been shown to be an important virulence factor (S. Lukomski, S. Sreevatsan, C. Amberg, W. Reichardt, M. Woischnik, A. Podbielski, and J. M. Musser, J. Clin, Invest, 99:2574-2580, 1997). Genetic inactivation of SpeB significantly decreased the lethality of a serotype M49 strain for mice and abolished the lethality of a serotype M3 strain after intraperitoneal (i.p.) **injection**, In the present study, a wild-type M3 isolate and an M3 speB mutant derivative were used to investigate the mechanism responsible for altered virulence, Following i.p. **injection**, the mutant and wild-type strains induced virtually identical cellular inflammatory responses, characterized largely by an influx of polymorphonuclear leukocytes (PMNs), In addition, the mutant and wild-type strains rapidly entered the blood and were recovered from all organs examined, However, significantly fewer ($P < 0.05$) CFUs of the isogenic mutant derivative than of the wild-type parent strain were recovered from blood and organs, PMNs effectively cleared the M3 speB mutant from the peritoneum by 22 h, thereby sparing the host, In contrast, the wild-type M3 strain continued to replicate intraperitoneally and had the ability to kill phagocytes, This process allowed the wild-type strain to continuously disseminate, resulting in host death, Our results indicate that genetic inactivation of the cysteine protease decreased the resistance of the mutant to phagocytosis and impaired its subsequent dissemination to organs, These results provide insight into the detrimental effect of SpeB inactivation on virulence.
AN 1998:114599 SCISEARCH
GA The Genuine Article (R) Number: YU693
TI Genetic inactivation of an extracellular cysteine protease (SpeB) expressed by **Streptococcus** pyogenes decreases resistance to phagocytosis and dissemination to organs
AU Lukomski S; Burns E H; Wyde P R; Podbielski A; Rurangirwa J; MoorePoveda D K; Musser J M (Reprint)
CS BAYLOR COLL MED, DEPT PATHOL, INST STUDY HUMAN BACTERIAL PATHOGENESIS, 1 BAYLOR PLAZA, HOUSTON, TX 77030 (Reprint); BAYLOR COLL MED, DEPT PATHOL, INST STUDY HUMAN BACTERIAL PATHOGENESIS, HOUSTON, TX 77030; BAYLOR COLL MED, DEPT MICROBIOL & IMMUNOL, HOUSTON, TX 77030; UNIV ULM, DEPT MED MICROBIOL, D-89069 ULM, GERMANY
CYA USA; GERMANY
SO INFECTION AND IMMUNITY, (FEB 1998) Vol. 66, No. 2, pp. 771-776. Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 33
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 15 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB An M2 **streptococcal** isolate and isogenic mutants in which either the emm or mrp gene was insertionally inactivated were tested for virulence using either a mouse model or a chicken embryo model. The results of the studies using the mouse model demonstrated that neither the emm nor mrp gene products had a significant effect on virulence when mice were challenged via the i.p. route. However, when the bacteria were **injected** into the skin the emm gene product was identified as a virulence factor. In parallel studies in the chicken embryo model the mrp gene product was found to be a major virulence factor, while a minor contribution to virulence could also be attributed to the emm gene

product. The importance of these gene products to virulence was noted when the chicken embryo were **injected** either i.v or when the bacteria were placed on top of the chorioallantoic membrane. The direct comparison of a single wild type group A organism and its paired isogenic mutants in two animal models suggests that different combinations of bacterial factors are required to overcome host defense strategies associated with different animal species. (C) 1997 Academic Press Limited.

AN 1998:120721 SCISEARCH
GA The Genuine Article (R) Number: YV075
TI Inactivation of single genes within the virulence regulon of an M2 group A **streptococcal** isolate results in differences in virulence for chicken embryos and for mice
AU Schmidt K H; Podbielski A; Raeder R; Boyle M D P (Reprint)
CS MED COLL OHIO, DEPT MICROBIOL & IMMUNOL, 3000 ARLINGTON AVE, TOLEDO, OH 43699 (Reprint); MED COLL OHIO, DEPT MICROBIOL & IMMUNOL, TOLEDO, OH 43699; HOSP JENA, INST MED MICROBIOL, D-07740 JENA, GERMANY; UNIV ULM, D-89081 ULM, GERMANY
CYA USA; GERMANY
SO MICROBIAL PATHOGENESIS, (DEC 1997) Vol. 23, No. 6, pp. 347-355. Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON, ENGLAND NW1 7DX. ISSN: 0882-4010.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 16 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB The group C streptococci are the most commonly isolated bacteria from disease states in the horse. Important virulence factors of S. equi and S. zooepidemicus are the **hyaluronic acid** capsule and the antiphagocytic fibrillar M protein located on the surface of the cell wall and extending into and through the capsule. The **hyaluronic acid** capsule is non-antigenic and so is not involved in protective immunity. The M protein, a superantigen, elicits very strong B and T cell responses that may result in protective immunity mediated by opsonic antibodies in plasma and by locally synthesized IgG and IgA on the pharyngeal mucosa. However, vaccines based on acid or mutanolysin extracted M protein do not confer a high level of protection against field exposure. Protective antibodies to S. equi or S. zooepidemicus can in part be assayed by the bactericidal test that measures opsonization for equine neutrophils. A mouse-challenge model has also been used to test **immunizing** potency of **streptococcal** extracts and in a passive protection test for protective antibody. There is as yet no means of distinguishing protective opsonic or mucosal antibodies from other antibodies produced against the many epitopes on the M molecule.
AN 94:12688 SCISEARCH
GA The Genuine Article (R) Number: MM915
TI THE PROTECTIVE M-PROTEINS OF THE EQUINE GROUP-C STREPTOCOCCI
AU TIMONEY J F (Reprint); MUKHTAR M M
CS UNIV KENTUCKY, GLUCK EQUINE RES CTR, LEXINGTON, KY, 40506 (Reprint); UNIV KHARTOUM, DEPT PREVENT MED, KHARTOUM, SUDAN
CYA USA; SUDAN
SO VETERINARY MICROBIOLOGY, (NOV 1993) Vol. 37, No. 3-4, pp. 389-395. ISSN: 0378-1135.
DT Article; Journal
FS LIFE; AGRI
LA ENGLISH
REC Reference Count: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 17 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB In an attempt to more fully understand the generation of antibody diversity to carbohydrate (CHO) Ag, we produced and characterized a panel

of hybridoma cell lines specific for group A **streptococcal** CHO from mice **injected** with the intact bacteria (minus the **hyaluronic acid** capsule and cell wall protein Ag). We have analyzed the use of H and L chain V region genes in the early (day 7) and late response (hyperimmune) and have sequenced the dominant VH gene used in several of our hybridomas. Our data allowed us to assess the extent to which the recombination of various V, D, and J gene segments and somatic mutation contribute to antibody diversification in this system. In this report we confirm that a minimum of two VH and four VK gene segments are used to encode this response. We extend this analysis to show that multiple D and J gene segments are used and that a significant amount of junctional variability is tolerated in CDR 3. Our results indicate that the level of somatic mutation in the hyperimmune response is generally low in comparison with the response to haptens and protein Ag. These data also suggest that there is a positive selection for mutation in CDR 1 during the hyperimmune response to group A **streptococcal** CHO.

AN 1990:89309 BIOSIS
DN BA89:48660
TI MOUSE ANTIBODY RESPONSE TO GROUP A **STREPTOCOCCAL** CARBOHYDRATE.
AU JARVIS C D; CANNON L E; STAVNEZER J
CS UNIV. MASSACHUSETTS MED. SCH., DEP. MOL. GENETICS AND MICROBIOL., 55 LAKE AVE. N., WORCESTER, MASS. 01655.
SO J IMMUNOL, (1989) 143 (12), 4213-4220.
CODEN: JOIMA3. ISSN: 0022-1767.
FS BA; OLD
LA English

L7 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB The immunogenicity of **hyaluronic acid** was investigated. Rabbits were **immunized** with encapsulated group A and C streptococci. Intact long-chain hyaluronate was conjugated to BSA for use as antigen in an ELISA. Antibodies to the hyaluronate-BSA conjugate were detected in peak immune sera. The specificity of the antibodies for both mammalian and **streptococcal** hyaluronate was shown by inhibition studies. To further confirm the presence of antihyaluronate antibodies, hyaluronidase-digested **streptococcal** hyaluronate was conjugated to biotin and used as an antigen in the ELISA. A clear **immunization** effect was shown for each rabbit by the study of preimmune and postimmunization bleedings. Titers for each rabbit increased by > 32-256-fold. Inhibition studies using hyaluronidase-digested hyaluronate and periodate-treated hyaluronate showed that the immunodominant site of antibody reactivity was a terminal glucuronic acid residue. Further studies showed that the carboxyl group of the terminal glucuronide was the major immunoreactive site. Both mammalian and **streptococcal** hyaluronate inhibited the immune rabbit sera reaction to **streptococcal** hyaluronate, demonstrating crossreactivity of these molecules. Thus, hyaluronate was shown to be immunogenic in rabbits.

AN 1986:454945 BIOSIS
DN BA82:111787
TI INDUCTION OF ANTIBODIES TO **HYALURONIC-ACID** BY **IMMUNIZATION** OF RABBITS WITH ENCAPSULATED STREPTOCOCCI.
AU FILLIT H M; MCCARTY M; BLAKE M
CS LAB. BACTERIOLOGY IMMUNOLOGY, ROCKEFELLER UNIV., NEW YORK, N.Y. 10021.
SO J EXP MED, (1986) 164 (3), 762-776.
CODEN: JEMEAV. ISSN: 0022-1007.
FS BA; OLD
LA English

L7 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB **Streptococcal** pyrogenic exotoxin type B purified from culture filtrates of the NY-5 or T-19 strain of group A **streptococcus** was heterogeneous in charge. Three protein fractions with isoelectric points of 8.0, 8.4 and 9.0 were isolated by differential solubility in

ethanol and acetate-buffered saline followed by isoelectric focusing and shown to be antigenically identical to **streptococcal** pyrogenic exotoxin type B. The MW of all 3 fractions were approximately 17,500, as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, with aggregates forming in the presence of **hyaluronic acid**. Only the pI [isoelectric point] 8.4 fraction showed the characteristic activities of **streptococcal** pyrogenic exotoxin in rabbits: pyrogenicity and ability to enhance susceptibility to lethal endotoxin shock. The pI 8.0 and pI 9.0 fractions were not pyrogenic, but could be used to **immunize** against pyrogenicity. These 2 fractions failed either to enhance lethal endotoxin shock or to **immunize** against enhancement activity. When the isolated fractions were electrofocused again they appeared heterogeneous, suggesting an instability of the B toxin molecular forms.

AN 1978:229439 BIOSIS
DN BA66:41936
TI HETEROGENEITY OF GROUP A **STREPTOCOCCAL** PYROGENIC EXO TOXIN TYPE B.
AU BARSUMIAN E L; CUNNINGHAM C M; SCHLIEVERT P M; WATSON D W
CS DEP. MICROBIOL., UNIV. MINN., MINNEAPOLIS, MINN. 55455, USA.
SO INFECT IMMUN, (1978) 20 (2), 512-518.
CODEN: INFIBR. ISSN: 0019-9567.
FS BA; OLD
LA English

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1: J Periodontol. 1999 Apr;70(4):370-4. Related Articles, Links

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Bacteriostatic effects of hyaluronic acid.

Pirnazar P, Wolinsky L, Nachnani S, Haake S, Pilloni A, Bernard GW.

Section of Oral Biology, UCLA School of Dentistry, Los Angeles, CA 90024, USA.

BACKGROUND: This investigation is one of a series of projects seeking to ascertain whether hyaluronic acid (HA) is therapeutically effective in tissue regeneration procedures. The rationale for these investigations is to test the hypothesis that HA can serve as a bioabsorbable carrier for other substrates as well as itself actively promote the regeneration of tissue. METHODS: In this paper, we report on the bacteriostatic and bactericidal properties of 3 molecular weight formulations of recombinant HA (low, 141 kD; medium, 757 kD; and high, 1,300 kD) on selected oral and non-oral microorganisms in the planktonic phase. Three concentrations of each HA formulation were screened, 0.5, 1.0, and 2.0 mg/ml, using a standard broth culture assay. RESULTS: Recombinant HA exerted varied bacteriostatic effects on all the bacterial strains tested depending on its molecular weight (MW) and concentration. The high concentrations of the medium MW HA had the greatest bacteriostatic effect, particularly on the Actinobacillus actinomycetemcomitans, Prevotella oris, Staphylococcus aureus, and Propionibacterium acnes strains. The 1.0 mg/ml concentration of high MW HA had the greatest overall bacteriostatic effect, inhibiting the growth of all 6 bacterial strains tested. Among the bacterial strains studied, HA was found to have no bactericidal effects, regardless of concentration or molecular weight. CONCLUSIONS: The results of this study suggest that HA in the MW range of 1,300 kD may prove beneficial in minimizing bacterial contamination of surgical wounds when used in guided tissue regeneration surgery.

PMID: 10328647 [PubMed - indexed for MEDLINE]

22 ANSWER 24 OF 27 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB The present study was designed to comparatively investigate 34 beta-hemolytic streptococci isolated from infected pigs and monkeys from various islands in Indonesia. According to the serological and biochemical data, all 34 isolates were Lancefield's serological **group C** streptococci and could be identified as **Streptococcus** equi subsp, zooepidemicus. Of the 34 **group C** streptococci investigated, 28 grew on solid media in large, mucoid colonies, in fluid media at a uniform turbidity, and in soft agar in diffuse colonies. A decapsulation test with a hyaluronidase-producing Staphylococcus aureus strain revealed the **hyaluronic acid** nature of the capsular material. The remaining six streptococci grew on solid media in small, nonmucoid colonies, in fluid media as sediment with clear supernatant, and in soft agar in compact colonies. Determination of surface hydrophobicity by salt aggregation revealed a hydrophilic surface for the encapsulated bacteria and a hydrophobic surface for the unencapsulated **group C** streptococci. To further analyze the epidemiological relationships, all 34 mucoid and nonmucoid isolates from pigs and monkeys were subjected to protein and DNA fingerprinting. The latter was performed by pulsed-field gel electrophoresis. The protein profiles of all 34 isolates and the DNA profiles of 32 isolates appeared to be identical, with the DNA profiles of 2 isolates being closely related, indicating that a single virulent clone is responsible for this disease outbreak in Indonesia.

AN 96:637797 SCISEARCH

GA The Genuine Article (R) Number: VD335

TI IDENTIFICATION AND MOLECULAR CHARACTERIZATION OF SEROLOGICAL **GROUP -C** STREPTOCOCCI ISOLATED FROM DISEASED PIGS AND MONKEYS IN INDONESIA

AU SOEDARMANTO I; PASARIBU F H; WIBAWAN I W T; LAMMLER C (Reprint)

CS UNIV GIESSEN, INST BAKTERIOL & IMMUNOL, FRANKFURTER STR 107, D-35392 GIESSEN, GERMANY (Reprint); UNIV GIESSEN, INST BAKTERIOL & IMMUNOL, D-35392 GIESSEN, GERMANY; BOGOR AGR UNIV, FAC VET MED, BOGOR, INDONESIA

CYA GERMANY; INDONESIA

SO JOURNAL OF CLINICAL MICROBIOLOGY, (SEP 1996) Vol. 34, No. 9, pp. 2201-2204.
ISSN: 0095-1137.

DT Article; Journal

FS LIFE; CLIN

LA ENGLISH

REC Reference Count: 26

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

ANSWER 67 OF 85 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11

AB Toxic shock syndrome continues to be encountered more frequently with the head and neck areas as sources of the toxin. In head and neck surgery practice it is most commonly noted following nasal packing. An unusual case associated with **staphylococcal pharyngitis** and spontaneous submandibular space abscess is reported and the literature concerning the subject is reviewed. **Treatment** is eradication of the infective focus, aggressive support of vital functions, and parenteral antistaphylococcal antibiotics.

AN 1991:388277 BIOSIS

DN BA92:65592

TI TOXIC SHOCK SYNDROME ASSOCIATED WITH **PHARYNGITIS** AND SUBMANDIBULAR SPACE ABSCESS.

AU SALES J H; KENNEDY K S; GALANTICH P T; GOMEZ P J

CS DEP. OTOLARYNGOL.-HEAD NECK SURG., NAVAL HOSP., PORTSMOUTH, VA. 23708-5100.

SO ANN OTOL RHINOL LARYNGOL, (1991) 100 (7), 540-543.
CODEN: AORHA2. ISSN: 0003-4894.

FS BA; OLD

LA English

L9 ANSWER 16 OF 25 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB Staphylococcus aureus is a causative agent of community-acquired respiratory tract infections. Rhinopharyngeal carriage is relatively common and this must be taken into account in the microbiological diagnosis. The frequency of **pharyngitis** and rhinopharyngitis due to S. aureus is therefore difficult to evaluate but is probably significant. S. aureus is the most frequently encountered organism in paediatric bacterial tracheitis and is responsible for 2-7.5 % of cases of acute sinusitis and 9 % in acute otitis media. Its involvement in pneumonia is increasing, particularly in the elderly and immunodepressed subject (1-14 %, mean 4-5 %). Whether S. aureus is blood- or airborne is unknown, but it often superinfects viral lesions. A number of cases of toxic shock syndrome have been reported during both benign and severe respiratory tract infections due to S. aureus. Strains acquired in the community are generally sensitive to penicillinase-resistant antibiotics such as cefuroxime axetil.

AN 91:621405 SCISEARCH
GA The Genuine Article (R) Number: GN643

TI **STAPHYLOCOCCAL** COMMUNITY-ACQUIRED RESPIRATORY-TRACT INFECTIONS

AU FLEURETTE J (Reprint)
CS FAC MED ALEXIS CARREL, CTR NATL REFERENCE STAPHYLOCOQUES, RUE GUILLAUME PARADIN, F-69372 LYONS 08, FRANCE (Reprint)
CYA FRANCE

SO MEDECINE ET MALADIES INFECTIEUSES, (1991) Vol. 21, pp. 27-33.
DT Article; Journal
FS CLIN
LA French
REC No References Keyed